quality of clinical evidence originating from same studies has been rated differentially by different agencies. The economic evidence in this area was primarily based on cost-effectiveness/cost utility analysis (CEA/CUA), comprising ~95% of studies (time horizon 50 years to lifetime). The incremental cost-effectiveness ratios (ICER) ranged USD15000-200000 in PBAC, USD1246-376723 in NICE, USD750-45200 in SMC, and USD11000-75000 in CADTH. More than 90% of the decisions based on ICER values were positive, with restriction being focused on cost negotiations. The primary driver of positive decisions was majorly economic analysis in NICE, PBAC, and SMC, while clinical evidence drove positive recommendations in CADTH, IQWiG, and HAS. **CONCLUSIONS:** Current landscape of CHC treatments in Canada, Australia, UK, Scotland, Germany, and France is majorly dominated by positive recommendations, considering the high unmet in this area. Most of the restrictions were around cost negotiations. The drivers of decisions fit with agency priorities, with economic analysis being the key driver in agencies with pharmacoeconomic analysis, and clinical evidence in agencies without pharmacoeconomic analysis.

PGI59

COMPARISON OF REGULATORY LABELS AND HTA DECISIONS FOR CHRONIC HEPATITIS-C THERAPIES

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OBJECTIVES: To compare the regulatory label indications and health technology assessment (HTA) recommendations for therapies indicated for the treatment of chronic hepatitis-C (CHC). **METHODS:** We reviewed the regulatory labels approved by European Medicines Agency (Europe), Health Canada (Canada) and Therapeutic Goods Administration (Australia). HTA reports for CHC therapies published by NICE (England and Wales), SMC (Scotland), HAS (France), IQWiG (Germany), CADTH (Canada) and PBAC (Australia) were assessed. Therapies with a positive HTA decision (recommended or restricted) were included in the analysis. Indication was split into four categories: age of the population (children, adults or both), fibrosis status (cirrhotic or non-cirrhotic), genotype, and prior treatment history (naïve or treatment-experienced). A match was defined as overlap of HTA and regulatory decision for any of the categories. Percentage correlation of the HTA indication with the regulatory label was calculated as the ratio of actual matches to the maximum possible matches for the parameters considered. **RESULTS:** A total of 34 regulatory approvals and 48 HTA reports were identified from the public domain. Forty-six HTA reports providing a positive decision were included. Overall, HTA decisions correlated well with the marketing authorization (89%), with the highest correlation observed for CADTH and PBAC (100% each), followed by HAS (98%), NICE and SMC (86% each) and IQWiG (63%). Across agencies, highest correlation was observed for age of the population (96% cases) and lowest for the prior treatment history (85% cases) of the population for whom the therapies were recommended. **CONCLUSIONS:** Overall, the indication approved by HTA agency almost correlated completely with the indication granted marketing authorization, except for NICE, SMC and IQWiG, indicating difference in agency priorities driving HTA decisions. Analyzing the population restriction applied by NICE, SMC and IQWiG would provide the decision drivers, allowing manufacturers to address these concerns in prospective submissions.

PGI60

TRENDS IN HEALTH TECHNOLOGY ASSESSMENT DECISIONS ACROSS THE GLOBE: A FOCUS ON HEPATITIS C

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OBJECTIVES: Recent advances in the management of hepatitis C virus (HCV) have yielded therapeutic modalities that are more efficacious, better tolerated, and have a lower pill and injection burden. Given the large population affected by HCV, decisions by health technology assessment (HTA) bodies weigh significantly in terms of societal benefits and expenditures. The objective of this analysis was to evaluate recent patterns in HCV-related HTA decisions in selected countries. **METHODS:** HTA surveillance was conducted for Australia, Canada, France, Germany, and the United Kingdom (UK) from January 1, 2012 to June 1, 2015 (42 months). HTAs for HCV treatments were evaluated by genotype, decision, and decision rationale. Decisions were categorized as favorable, unfavorable, mixed (both favorable and unfavorable), and neutral (deferral). **RESULTS:** 32 HCV-related HTAs were published in the study time frame, with 7 assessments currently in development. Among the completed assessments, the majority of decisions were favorable (24, 75%), with only 2 (6%) unfavorable and 6 (19%) mixed decisions. The most common rationales provided for a negative decision included insufficient data and/or inappropriate comparators (4), insufficient benefit to justify the high cost (ie, improperly high incremental cost-effectiveness ratio [ICER]) (3), and inadequate clinical benefit vs the most appropriate comparator (1). France and Canada had the highest percentage of favorable decisions (5 of 5 and 9 of 9, respectively, 100%), followed by the UK (3 of 4, 75%), Australia (5 of 8, 63%), and Germany (2 of 6, 33%). **CONCLUSIONS:** Based on the last 42 months of HCV-related HTAs, 75% of decisions were favorable. However, the most significant factors leading to unfavorable assessments for HCV products are related to the inability to supply advantageous clinical and cost-effectiveness data. This analysis suggests that manufacturers would have greater success with HTA decisions if more robust health economic and clinical data are generated.

PGI61

BIOLOGICS IN ULCERATIVE COLITIS (UC): TREATMENT GUIDELINES AND HEALTH TECHNOLOGY ASSESSMENTS (HTA)

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OBJECTIVES: To review clinical guidelines, recent HTA decisions, and the influence of economic analyses in HTA decisions related to biologic therapies in UC. **METHODS:** A literature review and targeted research provided information on clinical treatment guidelines (US and Europe) and HTAs (Europe) related to biologics in UC. Economic models in UC were identified and reviewed to determine how these affected HTA decisions. **RESULTS:** Since several biologics were approved after the last version of the US treatment guidelines, the US guidelines only address the use of infliximab for the treatment of moderate or severe UC. In the UK, NICE has recommended infliximab, adalimumab, and golimumab as possible treatments for adults with moderate to severe UC in whom conventional therapy hasn't worked or isn't suitable. A recent NICE HTA recommends vedolizumab as an option for treating moderately to severely active UC in adults only if the company provides vedolizumab with the discount agreed in the patient access scheme. The Scottish Medicines Consortium (SMC) recommends vedolizumab for the treatment of adult patients with moderate-to-severe UC and an inadequate response, lost response, or intolerance to conventional therapy or a TNFα antagonist; this advice is "contingent upon the continuing availability of the patient access scheme in NHS Scotland or a list price that is equivalent or lower." Earlier SMC advice did not recommend adalimumab, golimumab or infliximab for use within NHS Scotland due to lack of robust economic analyses. The SMC advice is superseded by the NICE HTA decisions. **CONCLUSIONS:** In the UK and Scotland, more than 9 HTA have been performed in the 10 years since biologics have become available for the treatment of moderate-to-severe UC. Differential cost-effectiveness among specific indications, lines of treatment, and countries have resulted in a variety of recommendations as to their use which supplement clinical guidelines in UC.

PGI62

DOSE ESCALATION AMONG ULCERATIVE COLITIS PATIENTS TREATED WITH ADALIMUMAB IN SWEDEN

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OBJECTIVES: The objective of this study was to describe the real-world use of adalimumab (ADA) for maintenance treatment of ulcerative colitis (UC) on a national level in Sweden. **METHODS:** A longitudinal, retrospective cohort study was conducted using the National Drug Registry and the National Patient Registry. UC patients (age ≥18 years) treated with ADA were included. Two cohorts were selected: (1) ADA naïve patients and (2) a cross-sectional cohort. Both cohorts were followed for a 12-month period. Dose escalation among the ADA naïve patients was defined as doubling of dose (ADA 40 mg every week) or having two following filled prescriptions with average biweekly dose (ABD) ≥ 50 mg. Dosing in the cross-sectional cohort was assessed studying annual number of injections dispensed among patients on maintenance treatment. **RESULTS:** Five hundred and eighty-seven patients were identified as ADA naive during Jan 2010-April 2014. Dose-escalation by doubling of dose was observed in 273 (46.5%) patients with the median time to dose escalation being 84 days. Further analysis revealed that 191 patients (32.5%) in the ADA naive patient cohort dose-escalated defined as (ABD) ≥ 50 mg, and of these 40 (20.9%) had a subsequent dose de-escalation which occurred after a median time of 162 days. In total 992 UC patients were identified in the cross-sectional cohort, defined as filling at least one prescription during May 2013-April 2014, and of these 364 (37%) were on maintenance treatment. Out of the 364 patients on maintenance treatment dispensing at least 22 injections during the period 140 (38%) received 30 injections or more. **CONCLUSIONS:** This study demonstrates that UC patients receiving ADA in general have a patchy prescription pattern, and that the proportion of patients who dose escalate is high. This finding and the impact that dose escalation has on costs may have implications for healthcare professionals and budget holders.

PGI63

EFFECTS OF FINANCIAL INCENTIVES FOR SAVING DRUG EXPENDITURES ON PHYSICIAN PRESCRIPTION BEHAVIORS

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OBJECTIVES: The purpose of this study is to assess the impact on physician prescription behaviors of an outpatient prescription incentive program providing financial rewards to primary care physicians for saving prescription costs implemented in October 2010 in South Korea. **METHODS:** A 10% sample of clinics (N=1,625) was randomly selected from the entire clinics in the National Health Insurance claims database for the years 2009~2012, and all claims with the primary diagnosis of peptic ulcer or gastro-esophageal reflux diseases were extracted from those clinics' data. We used a clinic-level random effects model analyzing policy effects on drug expenditures and prescribing behaviors including prescription rate of medicines treating target diseases, number of drug prescribed per claim, prescription duration per claim. We also performed subgroup analyses by selected clinic characteristics, including practice type, size and specialty. **RESULTS:** We found no significant impact of the program on drug expenditure overall. Prescription rate of target medicines increased and the average prescription duration per claim decreased after the incentive program. After the financial incentive program, clinics in general medicine showed a lower prescription rate (by 0.8 percentage points), lower number of medicines prescribed (by 0.02), a lower prescription duration (by 0.15 days), and lower drug expenditure per claim after the policy (by 740 won). Small clinics had shorter prescription duration (by 0.76 days), while large clinics and clinics in group practice had a higher prescription rate (by 1.5 and 2.5 percentage points, respectively) and higher number of medicines prescribed (by 0.03 for group practice only) after the program. **CONCLUSIONS:** The financial incentive program worked as intended only in certain subgroup clinics for the target medicines. The reduction in prescription duration and the number of prescribed medicines in target claims in selected subgroups imply some margin for prescription adjustments.

MUSCULAR-SKELETAL DISORDERS – Clinical Outcomes Studies

PMS1
THE EFFECT OF POSITIONING THE LOWER EXTREMITIES ON POSTOPERATIVE BLEEDING AFTER TOTAL KNEE REPLACEMENT

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OBJECTIVES: Postoperative blood-saving is high-priority after every planned surgery. The aim of this study was to analyse the effect of positioning of lower extremities on the postoperative bleeding after total knee replacement surgery. **METHODS:** Sixty patients from the orthopaedic department of Zala County Hospital who were operated on for insertion of a unilateral total knee prosthesis with cement and got autologous blood transfusion (age 35-80 years), were randomly assigned to three intervention groups. In Group I (n=20), patients were in normal laying position, in Group II (n=20), hips were positioned in flexion and knee in extension and in Group III (n=20), hips and knees were positioned in 30o flexion in the first 6 postoperative hours. The surgical technique, the surgeon and the anticoagulant treatments were the same. Data collection: medical records, haemoglobin and haematocrit. For the clinical parameters, t-tests, ANOVA and Scheffe post hoc tests were used. Statistical significance was established at the α-level of 0.05, and IBM SPSS 20.0v was used. **RESULTS:** During the first six postoperative hours positioning not affected significantly on the volume of bleeding and recirculated blood volume (Group I: 615.0±247.3, Group II: 600.0±358.2, Group III: 715.0±392.3 ml, ANOVA: p=0.714; post hoc: p1-2=0.995, p1-3=0.805, p 2-3=0.751), either in hours 6-72 (Group I: 775.0±227.6, Group II: 762.0±332.8, Group III: 960.0±400.6 ml, p=0.335; p1-2=0.996, p1-3=0.462, p2-3=0.414). Most units of homologous transfusion were needed in Group II (10 units). Position had not effect on the intensity of pain and value of the active range of motion of the knee (p= 0.682 vs. p = 0.585) either in haemoglobin and haematocrit values (p=0.362 vs. p=0.559). **CONCLUSIONS:** These results of the present study suggest that the postoperative positioning of the lower extremities after knee replacement not affected the postoperative bleeding, the pain and the range of motion of the knee joint.

PMS2
RHEUMATOID ARTHRITIS AND ISCHEMIC HEART DISEASE IN PATIENTS FROM BLUMENAU - BRAZIL

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OBJECTIVES: Patients with rheumatoid arthritis (RA) have a higher risk of ischemic cardiac events compared with the general population. This would be explained not only by the greater presence of traditional risk factors, but also by the systemic inflammatory nature of arthritis. To compare the prevalence of ischemic heart disease (IHD) in a target RA population with the international prevalence data. **METHODS:** Cross-sectional study including 183 adult patients with code M05-M06 (ICD-10) attended in primary or secondary care units from Blumenau city, southern Brazil, in 2014. Data collection was performed through structured personal interview and, if necessary, later by phone. The presence of IHD was defined as acute myocardial infarction, unstable angina, percutaneous coronary intervention or coronary artery bypass graft that have occurred after the diagnosis of RA. **RESULTS:** 153/183 patients were female (83.6%), mean age of 56.9 years and disease mean duration of 12.1 years. The number of cases with first acute myocardial infarction, unstable angina or myocardial revascularization after the diagnosis of rheumatoid arthritis was 7 (3.8%), two men and five women, two of those fatal, one of each sex. When the international prevalence are in Denmark 2.6%, Sweden 3.3%, Netherlands 3.8%, UK 4.8%, France 4.1%, Canada 3.5%, US 3.7%, China 3.5%, Russia 5.1%, New Zealand 5.2%. **CONCLUSIONS:** The result shows that the prevalence of coronary ischemia in patients with rheumatoid arthritis from Blumenau is similar to the prevalence observed in other countries.

PMS3
INCREASED RISK OF OSTEOPOROSIS IN DEPRESSED PATIENTS: A REAL WORLD DATA STUDY CONDUCTED IN ITALY

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OBJECTIVES: Depression is a chronic debilitating disease with high prevalence that considerably affects quality of life. The relationship between depression and osteoporosis has been demonstrated, but the evidence is heterogeneous. The aim of the present study is to investigate about this relationship in the Italian primary care setting. **METHODS:** This was a retrospective analysis based on data extracted from Italian IMS Health Longitudinal Patient Database. Two cohorts have been defined: patients with a diagnosis of Depression (Index Date) during the period January 2004 - December 2010 and without neither Depression neither Osteoporosis diagnosis during the 5 years period preceeding the Index Date; patients with a first contact (Index Date) during the period January 2004 - December 2010 that are not in the previous cohort (free from Depression) and without neither Osteoporosis neither Depression diagnosis during the five years period preceeding the Index Date. Patients in both the two cohorts have been followed-up until one of the following event occurred first: Osteoporosis diagnosis registration, death, end of registration with the GP, 31 December 2013. Osteoporosis incidence rates have been separately calculated in the two cohorts and Osteoporosis cumulative incidence curves have been estimated using Kaplan Meier methods and compared performing log rank tests. Both univariate and multivariate Cox proportional hazard models were performed. **RESULTS:** Osteoporosis incidence was higher in the cohort of depressed patients (2.33 cases per 100 person years vs 1.22 cases per 100 person years) and results were confirmed by the log rank test (p<0.001). Increased risk of developing osteoporosis for depressed patients was shown both by univariate proportional hazard model (HR=1.75, CI=[1.72,1.78]) and multivariate proportional hazard model (HR=1.15, CI=[1.13, 1.17]). **CONCLUSIONS:** Results from this study suggests that the relationship between Depression and Osteoporosis is confirmed also in the primary care setting in Italy.

PMS4
APPLYING WEIGHTED CUMULATIVE EXPOSURE MODELS TO PATTERNS OF NONSPECIFIC SYMPTOM CONSULTATIONS FOR EARLY DIAGNOSIS: A PRIMARY CARE DATABASE STUDY OF KNEE PAIN AND OSTEOARTHRITIS

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OBJECTIVES: To develop and validate predictive models for estimating risk of early diagnosis of knee osteoarthritis (OA) by weighted cumulative exposure (WCE) function scores of prior knee pain consultations. **METHODS:** Both derivation and validation datasets were from an electronic healthcare record (EHR) database (Consultations in Primary Care Archive [CiPCA]) in England. WCE functions for modelling cumulative effect of time-varying knee pain consultations weighted by recency was derived as predictive tool in a population based case-control sample and validated in a prospective cohort sample. Two sets of WCE function scores: WCE (Half-Normal) score and WCE (Spline) score were evaluated and compared on model fitness, discrimination, and calibration both in derivation and validation phases. **RESULTS:** People with the most recent and the most frequent knee pain consultations were more likely to have high WCE scores (both sets) and these were associated with increased risk of knee OA diagnosis both in derivation and validation phases. Better model fit, discrimination, and calibration were observed for models with WCE (Spline). **CONCLUSIONS:** WCE functions can be used to model pre-diagnostic symptoms within routine EHR data and may provide novel low-cost predictive tools that may contribute to early diagnosis.

PMS5
CLINICAL EFFECTIVENESS OF BISPHOSPHONATES FOR PREVENTION OF FRAGILITY FRACTURES: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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OBJECTIVES: To assess the relative efficacy of bisphosphonates (alendronate, risedronate, ibandronate and zoledronate) for the treatment of Osteoporosis using network meta-analysis (NMA). **METHODS:** A systematic review of the literature was conducted using PRISMA guidelines. A network meta-analysis was used to determine the relative efficacy of treatments on four fracture outcomes (vertebral, non-vertebral, hip and wrist) and percentage change in femoral neck bone mineral density (BMD). Treatment effects were modelled using an exchangeable treatment effects model. Heterogeneity in treatment effects was explored by considering potential treatment effect modifiers using meta-regression. Where appropriate, inconsistency between direct and indirect evidence was assessed using node-splitting. **RESULTS:** 46 randomised controlled trials (RCTs) were identified. Twenty seven RCTs provided fracture data and 35 RCTs provided BMD data for analysis. Zoledronate was associated with the greatest treatment effect on vertebral fractures (HR 0.41, 95% CrI 0.28-0.56) and percentage change in BMD (3.21, 95% CrI 2.52-3.86) compared to Placebo. The greatest treatment effect on non-vertebral and wrist fractures was given by risedronate (HR 0.72, 95% CrI 0.53-0.89 and HR 0.77, 95% CrI 0.44-1.24, respectively). For hip fractures the greatest treatment effect was given by alendronate (HR 0.78, 95% CrI 0.44-1.30). **CONCLUSIONS:** All treatments were associated with beneficial effects on fractures and femoral neck BMD relative to placebo. For vertebral fractures and percentage change in BMD the treatment effects were statistically significant for all treatments. Pairwise comparisons between treatments indicated that no active treatment was statistically significantly more effective than any other active treatment for fracture outcomes. There was some heterogeneity in treatment effects between studies suggesting differential treatment effects according to study characteristics However, there was no evidence of differential treatment effects with respect to gender and age.

PMS6
COMPLIANCE WITH ALLOPURINOL AMONG HYPERTENSIVE PATIENTS WITH GOUT DIAGNOSIS AND THE RELATIONSHIP TO ONSET OF END-STAGE RENAL DISEASE

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OBJECTIVES: Risk of end-stage renal disease (ESRD) in both hypertension and gout has been examined in the literature. However, the impact of allopurinol adherence on primary prevention of ESRD has not been assessed. The objective is to evaluate impact of better allopurinol adherence on ESRD onset. **METHODS:** A cohort of 2752 patients with gout diagnosis was reconstructed using the Québec RAMQ and MED-ECHO administrative databases. New users of allopurinol, aged 45-85 years, with a diagnosis of hypertension and treated with an antihypertensive drug between 1997-2007 were eligible. A nested case-control design was used to study ESRD occurrence. Every ESRD case was matched for age, sex and duration of follow-up for up to 15 controls. Adherence level was assessed as medication possession ratio. Conditional logistic regression models were used to estimate rate ratios (RR) of ESRD adjusting for covariables. **RESULTS:** Patients had a mean age of 68 years, 82% were men, approximately 50% had ≥1 cardiovascular disorder, 33% had dyslipidemia, 21% had diabetes, 15% had chronic kidney disease, and 21%, 33%, and 42% were taking thiazides, low-dose aspirin, and NSAIDs, respectively. Clinical characteristics were similar among allopurinol adherent versus non-adherent patients. Major risk factor for ESRD onset was chronic kidney disease at stages 1-3 (RR: 8.00; CI: 3.16 -22.3), and hypertension severity (≥ 3 vs. < 3 antihypertensive treatments) was a trending risk factor as a crude estimate (RR: 1.94; CI: 0.68-5.51). Of 341 patients (cases, n=22; controls, n=319), high adherence (≥80%) to allopurinol, versus lower adherence (<80%), was associated with a lower rate of ESRD onset (RR: 0.35; confidence interval [CI]: 0.13-0.91). **CONCLUSIONS:** This population-based study suggests that better allopurinol adherence may be associated with risk reduction of new-onset ESRD in hypertensive patients. Further research is needed, as this study was limited by the small number of cases and potential residual confounding factors.